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Original Contribution

Correlates of Anemia in American Blacks and Whites

The REGARDS Renal Ancillary Study

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For unclear reasons, anemia is more common in American blacks than whites. The authors evaluated anemia prevalence (using World Health Organization criteria) among 19,836 blacks and whites recruited in 2003–2007 for the REasons for Geographic And Racial Differences in Stroke Renal Ancillary study and characterized anemia by 3 anemia-associated conditions (chronic kidney disease, inflammation, and microcytosis). They used multivariable models to assess potential causes of race differences in anemia. Anemia was 3.3-fold more common in blacks than whites, with little attenuation after adjusting for demographic variables, socioeconomic factors, and comorbid conditions. Increasing age, residence in the US southeast, lower income, vascular disease, diabetes, hypertension, and never smoking were associated with anemia. Age, diabetes, and vascular disease were stronger correlates of anemia among whites than blacks ($P < 0.05$). Among those with anemia, chronic kidney disease was less common among blacks than whites (22% vs. 34%), whereas inflammation (18% vs. 14%) and microcytosis (22% vs. 11%) were more common. In this large, geographically diverse cohort, anemia was 3-fold more common in blacks than whites with different characteristics and correlates. Race differences in anemia prevalence were not explained by the factors studied. Future research into the causes and consequences of anemia in different racial groups is needed.

anemia; chronic disease; health status disparities; kidney diseases; population groups

Abbreviations: CI, confidence interval; eGFR, estimated glomerular filtration rate; OR, odds ratio; REGARDS, REasons for Geographic And Racial Differences in Stroke.

A growing body of research suggests that anemia is independently associated with morbidity and mortality in the general population (1–4). American blacks have lower hemoglobin values than their white counterparts, with few studies exploring these racial differences or whether correlates of anemia differ between blacks and whites (1, 2, 5–13).

Although some of the racial differences in anemia prevalence may be due to inherited hemoglobin variants, common risk factors for anemia such as diabetes, hypertension, vascular disease, kidney disease, and socioeconomic factors differ by race (14). Despite recent improvements, achieving quality-of-care goals for vascular disease, diabetes, and hypertension is still worse among blacks, and the association of these conditions with anemia has not been well characterized in blacks and whites separately (15). Blacks are often underrepresented in epidemiologic studies, and there is almost no information on the role that comorbid conditions, socioeconomic factors, and demographics play in the increased prevalence of anemia in American blacks (16–18).

The REasons for Geographic And Racial Differences in Stroke (REGARDS) study is a national cohort of 30,228 subjects designed to study racial and geographic differences in stroke incidence in the United States (17). This study offers the opportunity to examine the role of demographic variables, socioeconomic factors, and medical conditions in explaining race differences in anemia prevalence and whether the correlates of anemia differ by race.

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MATERIALS AND METHODS

Participants

REGARDS participants were selected from a commercial, nationwide list of over 250 million individuals in the United States (Genesys Incorporated, Daly City, California) (17, 19). Between February 2003 and October 2007, 30,228 individuals were recruited, with approximately 50% of the cohort from the ''stroke belt'' (North Carolina, South Carolina, Georgia, Tennessee, Alabama, Mississippi, Arkansas, Louisiana), 50% black, and 50% female. A trained interviewer contacted and enumerated the household by telephone. One resident aged 45 years or older was randomly screened for eligibility; exclusion criteria were race other than black or white, active treatment for cancer, medical conditions preventing long-term participation, cognitive impairment as judged by the telephone interviewer, residence in or on a waiting list for a nursing home, and inability to communicate in English. Verbal informed consent and a medical history were collected. Afterward, participants underwent an in-home visit (Examination Management Systems Incorporated, Irving, Texas) for phlebotomy, urine collection, blood pressure measurement, anthropomorphic measures, and written informed consent. After recruitment of 8,400 participants, a complete blood count was added as part of the REGARDS Renal Ancillary study to evaluate the burden and complications of kidney disease. The response rate (the percentage agreeing to be interviewed among known eligible candidates contacted after adjustment for those of unknown eligibility) was approximately 41% (20). We included 19,893 participants enrolled through October 2007 for whom a complete blood count was available, excluding 57 participants with end-stage renal disease (total cohort of 19,836). This study was approved by the institutional review boards of the participating institutions.

Laboratory analysis

Phlebotomy was performed the morning of the in-home visit after a 10–12-hour fast. Samples were centrifuged, refrigerated, and shipped that night to the study laboratory at the University of Vermont. Upon arrival, samples were recentrifuged and analyzed for serum creatinine, glucose (Ortho Vitros 950IRC, Johnson & Johnson Clinical Diagnostics, Rochester, New York; coefficient of variation, 1.1% and 1%), and C-reactive protein (high-sensitivity particle-enhanced immunonephelometric assay on the BNII nephelometer, Dade Behring Incorporated, Deerfield, Illinois; coefficient of variation, 2.1%–5.7%) (21). After recruitment was complete, the REGARDS laboratory at the University of Vermont changed creatinine reagents to a method traceable to creatinine determined by isotope dilution mass spectrometry. Fifty samples (not REGARDS samples) were run in duplicate comparing the original method with the traceable method, yielding the following calibration equation: isotope dilution mass spectrometry traceable creatinine $= -0.0656 + 0.953 \times$ REGARDS creatinine. The 95% confidence intervals for the slope and intercept were 0.95, 0.96 and -0.09, -0.04, respectively, with a correlation coefficient of 0.9994. In addition, in 2007, 200 samples were sent from the REGARDS laboratory to the Cleveland Clinic for calibration, resulting in the following calibration equation: calibrated creatinine $= -0.06 + 0.98 \times$ REGARDS creatinine. Because the 2 equations were nearly identical, the isotope dilution mass spectrometry–traceable equation was used to calibrate the REGARDS creatinine values to calculate estimated glomerular filtration rate (eGFR) by using the following formula: eGFR $= 175 \times$ standardized creatinine$^{-1.154} \times$ age$^{-0.203} \times 1.212$ (if black) $\times 0.742$ (if female) (22).

Complete blood counts were performed by the central laboratory from an intact ethylenediaminetetraacetic acid tube using automated cell counting on a Beckman Coulter LH 755 Hematology Workcell (Beckman Coulter, Incorporated, Fullerton, California). Coefficients of variation between instruments and shifts were 5% for leukocyte count and 3% each for hemoglobin and mean corpuscular volume. The overall success rate for obtaining a hemoglobin concentration was 90.3%. Levels were measured the day after sample collection on 92.0% of samples and within 3 days on 95.8% of samples.

Definitions

The World Health Organization criteria were used to define anemia (hemoglobin <13 g/dL for men and <12 g/dL for women) (23). Race was determined from participant self-identification. Diabetes was defined as a fasting glucose level >126 mg/dL, a nonfasting glucose level >200 mg/dL, or a self-report of current treatment for diabetes. Hypertension was defined as blood pressure $>140/90$ mm Hg or self-report of current treatment for hypertension. Baseline vascular disease was defined as self-reported coronary, cerebrovascular, or peripheral artery disease, which included a self-report of stroke, transient ischemic attack, myocardial infarction/heart attack, coronary artery bypass graft/bypass surgery/graft, surgery on the arteries in the neck, angioplasty/stenting of a coronary artery, or procedure to repair the arteries in the leg. We considered 3 common anemia-associated conditions as explanatory variables for race differences in anemia: inflammation (cytokine-mediated bone marrow suppression), chronic kidney disease (erythropoietin deficiency), and microcytosis (nutritional deficiency or inherited hemoglobin variants). Inflammation was defined as C-reactive protein ≥ 10 mg/L or leukocyte count $\geq 15 \times 10^9$/L. Chronic kidney disease was defined as glomerular filtration rate <60 mL/minute per 1.73 m^2 calculated by using the 4-variable Modification in Diet in Renal Disease equation, unless otherwise noted (24). Microcytosis, normocytosis, and macrocytosis were defined as mean corpuscular volume ≤ 80 fL, 81–99 fL, and ≥ 100 fL, respectively.

Statistical analysis

The prevalence of anemia and average hemoglobin concentrations were evaluated by race and gender. Associations between risk factors and anemia status were evaluated by using χ^2 tests for categorical variables and 2-tailed t tests for continuous variables. For anemic individuals, χ^2 tests were

Table 1. Characteristics of the REGARDS Renal Ancillary Study by Race,[a] United States, 2003–2007

	All (n = 19,836)		White (n = 11,843)		Black (n = 7,992)	
	No.	%	No.	%	No.	%
Demographics[b]						
Age in years, mean (SD)	64.4 (9.7)		65.1 (9.8)		63.4 (9.5)	
Female gender	12,340	60	6,951	59	5,388	67
Black race	7,992	40				
Living in the stroke belt[c]	11,770	59	7,281	61	4,488	56
Socioeconomic variables[b]						
High school education	17,596	89	11,030	93	6,565	82
Annual income						
<$25,000	3,345	19	1,350	13	1,995	29
$25,000–$75,000	7,660	44	4,424	43	3,236	47
>$75,000	6,261	36	4,536	44	1,724	25
Medical conditions[b]						
Vascular disease	4,078	21	2,481	21	1,597	20
Diabetes	3,926	20	1,679	14	2,246	28
Hypertension	11,224	57	5,715	498	5,509	69
Ever smoker	10,347	52	6,166	52	4,180	53
Body mass index in kg/m^2, mean (SD)	29.4 (6.3)		28.3 (5.7)		31.0 (6.8)	
Anemia-associated conditions[b]						
Chronic kidney disease	2,095	11	1,324	11	770	10
Creatinine in mg/dL, mean (SD)	0.87 (0.33)		0.84 (0.25)		0.92 (0.42)	
Inflammation	1,848	9	789	7	1,059	13
Mean corpuscular volume						
Low (≤80 fL)	1,070	5	196	2	874	11
Normal (81–99 fL)	18,188	93	11,243	96	6,944	88
High (≥100 fL)	401	2	295	3	106	1

Abbreviations: REGARDS, REasons for Geographic And Racial Differences in Stroke; SD, standard deviation.

[a] Information on race was missing for 1 participant.

[b] Variables are defined in the Materials and Methods section of the text.

[c] North Carolina, South Carolina, Georgia, Tennessee, Alabama, Mississippi, Arkansas, Louisiana.

used to assess associations of the variables among blacks and whites. Incremental logistic regression models were used to examine the association of race with anemia and to evaluate for confounding. Model 1 was adjusted for demographic variables (age, gender, and region (southeast vs. elsewhere in the United States)). Model 2 added socioeconomic variables (high school graduation (yes, no), annual income (<$25,000, $25,000–$75,000, >$75,000)) to model 1, and model 3 added medical conditions (vascular disease, diabetes, hypertension, ever smoked, and body mass index) to model 2. Model 4 was run by including all the variables in the previous models as well as the 3 anemia-associated conditions (inflammation, chronic kidney disease, and microcytosis). Interactions between race and covariates were examined to assess for differential associations by race. Sensitivity analyses were conducted by using the Cockcroft-Gault equation rather than the Modification in Diet in Renal Disease equation to calculate glomerular filtration rate (because the latter equation includes a race term), excluding participants with microcytosis (to assess the impact of some nutritional deficiencies and α-thalassemia trait on associations) (24), and including the anemia-associated conditions (leukocyte count, C-reactive protein, mean corpuscular volume, eGFR) as continuous variables. Analyses were performed with SAS version 9.1 software (SAS Institute, Inc., Cary, North Carolina).

RESULTS

Characteristics of the 19,836 participants are shown in Table 1. There were 7,992 (40%) blacks and 11,843 (60%) whites, and 7,496 (38%) men and 12,340 (62%) women.

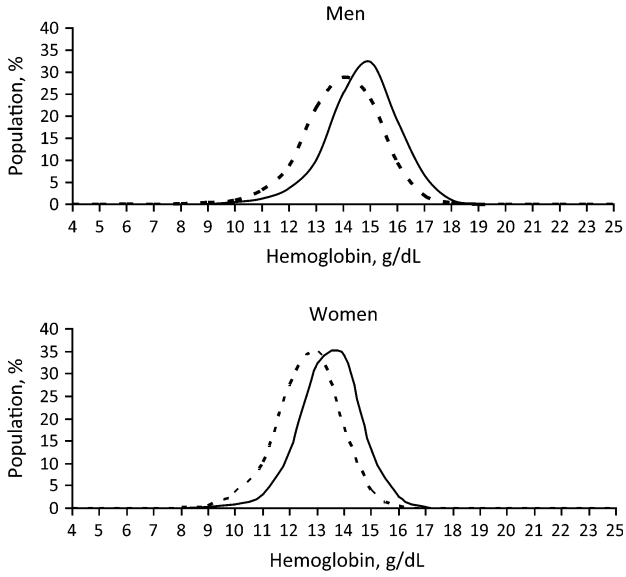

Figure 1. Distribution of hemoglobin concentration among black men and women (dashed lines) and white men and women (solid lines) (Bin is 1 g/dL) in the REGARDS Renal Ancillary Study, United States, 2003–2007.

Compared with whites, blacks had lower educational levels and income and a greater prevalence of diabetes, hypertension, and obesity. Blacks also had higher prevalences of inflammation and microcytosis. Prevalences of vascular disease, chronic kidney disease, and smoking were similar for blacks and whites.

Figure 1 shows the distribution of hemoglobin concentration by race-gender groups. For both men and women, blacks had lower hemoglobin levels than did whites, with no evidence for a skewed distribution in any race-gender stratum. As shown in Table 2, the overall anemia prevalence in the cohort was 14%, with a higher prevalence among blacks than whites (23% vs. 8%, $P < 0.001$). Women had a slightly higher prevalence of anemia than did men (15% vs. 13%, $P < 0.001$) mostly because of a higher prevalence of anemia among black women than black men (Table 2).

Table 3 shows the differences in characteristics of participants with and without anemia and these same characteristics by race among anemic participants. Compared with those without anemia, participants with anemia were older and had lower socioeconomic indicators (fewer high school graduates, lower annual income). Vascular disease, diabetes, hypertension, and higher body mass index were more common among those with than without anemia, whereas smoking was less common. Chronic kidney disease, inflammation, and microcytosis were more common among those with than without anemia (all $P < 0.001$).

When the 2 race groups of anemic participants were compared, blacks were younger than whites and had lower socioeconomic indicators. Although blacks with anemia had a higher prevalence of diabetes and hypertension than whites with anemia, they had a lower prevalence of vascular disease than whites with anemia. Compared with whites with anemia, blacks with anemia were less likely to have chronic kidney disease and more likely to have microcytosis (Table 3).

Table 4 shows a series of incrementally adjusted logistic regression models assessing for confounding or explanatory factors for the race differences in anemia prevalence. When the data were unadjusted, blacks had a 3.3-fold higher odds

Table 2. Prevalence of Anemia[a] and Hemoglobin Concentration by Race and Gender in the REGARDS Renal Ancillary Study, United States, 2003–2007

Race	Gender			*P* Value[b] (Male vs. Female)
	All (n = 19,836)	Male (n = 7,496)	Female (n = 12,340)	
All (n = 19,836)				
Anemia prevalence, no. (%)	2,809 (14)	958 (13)	1,851 (15)	<0.0001
Hemoglobin concentration in g/dL, mean (SD)	13.6 (1.5)	14.5 (1.4)	13.2 (1.2)	<0.0001
White (n = 11,843)				
Anemia prevalence, no. (%)	976 (8)	418 (9)	558 (8)	0.31
Hemoglobin concentration in g/dL, mean (SD)	14.0 (1.4)	14.8 (1.4)	13.5 (1.2)	<0.0001
Black (n = 7,992)				
Anemia prevalence, no. (%)	1,833 (23)	841 (21)	1,293 (24)	0.0012
Hemoglobin concentration in g/dL, mean (SD)	13.1 (1.4)	14.0 (1.4)	12.7 (1.2)	<0.0001
P value[a] (black vs. white)				
Anemia prevalence	<0.0001	<0.0001	<0.0001	
Hemoglobin concentration in g/dL	<0.0001	<0.0001	<0.0001	

Abbreviations: REGARDS, REasons for Geographic And Racial Differences in Stroke; SD, standard deviation.
[a] According to World Health Organization criteria used to define anemia.
[b] χ-square test of difference in proportions for anemia vs. nonanemia and 2-tailed t test for hemoglobin concentration.

Table 3. Characteristics of REGARDS Renal Ancillary Study Participants by Anemia Status, Overall and by Race, United States, 2003–2007

Characteristic[a]	Anemia					Anemic Subjects by Race				
	No (n = 17,027)		Yes (n = 2,809)		P Value (Anemia vs. no Anemia)	White (n = 976)		Black (n = 1,833)		P Value (White vs. Black)[b]
	No.	%	No.	%		No.	%	No.	%	
Demographics										
Age in years, mean (SD)	64.1 (9.7)		66.6 (10.4)		<0.001	69.2 (10.5)		65.3 (10.1)		<0.001
Female gender	10,489	62	1,851	66	<0.001	558	57	1,293	71	<0.001
Living in the southeast	9,999	59	1,771	63	<0.001	652	67	1,119	61	0.003
Socioeconomic variables										
High school education	15,306	90	2,290	82	<0.001	884	91	1,406	77	<0.001
Annual income					<0.001					<0.001
<$25,000	2,670	18	675	28		147	18	528	34	
$25,000–$75,000	6,508	44	1,152	48		414	50	738	48	
>$75,000	5,701	38	560	23		275	33	285	18	
Medical conditions										
Vascular disease	3,245	19	833	30	<0.001	358	37	475	26	<0.001
Diabetes	2,852	17	1,074	38	<0.001	322	33	752	41	<0.001
Hypertension	9,212	54	2,012	72	<0.001	612	63	1,400	77	<0.001
Ever smoker	8,992	53	1,355	48	<0.001	500	51	855	47	0.019
Body mass index in kg/m^2, mean (SD)	29.2 (6.2)		30.5 (7.1)		<0.001	28.5 (6.4)		31.5 (7.3)		<0.001
Anemia-associated conditions										
Chronic kidney disease	1,368	8	727	26	<0.001	334	34	393	22	<0.001
Inflammation	1,366	8	482	17	<0.001	134	14	347	19	<0.001
Mean corpuscular volume					<0.001					<0.001
Low (≤80 fL)	553	3	517	19		109	11	408	22	
Normal (81–99 fL)	15,993	95	2,195	79		815	84	1,380	76	
High (≥100 fL)	327	2	74	3		42	4	32	2	

Abbreviations: REGARDS, REasons for Geographic And Racial Differences in Stroke; SD, standard deviation.

[a] Definitions are provided in the Materials and Methods section of the text.

[b] P values reflect black-white differences in those with anemia, taking into account the different prevalences of the conditions by race in the entire cohort.

of anemia than whites (95% confidence interval (CI): 3.05, 3.60). The odds ratio was higher after adjustment for age, gender, and region (odds ratio (OR) = 3.64, 95% CI: 3.34, 3.97) and was slightly attenuated with additional adjustment for socioeconomic variables (OR = 3.27, 95% CI: 2.97, 3.60) and medical conditions (OR = 2.91, 95% CI: 2.63, 3.22). Further adjustment for anemia-associated conditions (chronic kidney disease, inflammation, and microcytosis) did not materially alter the increased odds of anemia for blacks compared with whites (OR = 2.78, 95% CI: 2.50, 3.10). In the sensitivity analyses, the fully adjusted association of black race with anemia was slightly lower when the Cockcroft-Gault equation was used to calculate eGFR (OR = 2.42, 95% CI: 2.18, 2.69) and was similar when participants with microcytosis were excluded from the analysis (OR = 2.76, 95% CI: 2.49, 3.06). Use of eGFR, mean corpuscular volume, leukocyte count, and C-reactive protein as continuous variables in these models did not materially change the main associations of race, socioeconomic conditions, and medical conditions with anemia (data not shown).

Associations of other risk factors with anemia are given in Table 4. Older age remained associated with anemia in all models, although the higher odds ratio of anemia for women was no longer significant after adjustment for demographic variables. Individuals in the stroke belt were marginally more likely to be anemic in demographic-adjusted models, with modest attenuation after adjustment for medical conditions and anemia-associated conditions. Education less than high school and annual income less than $75,000 remained associated with anemia in all models, although with attenuation after adjustment for demographic variables and medical conditions. Vascular disease, diabetes, and

Table 4. Multivariable Logistic Regression Models of Anemia Correlates in the REGARDS Renal Ancillary Study, United States, 2003–2007

	Unadjusted (n = 19,836)		Model 1[a] (n = 19,826)		Model 2[b] (n = 17,246)		Model 3[c] (n = 16,886)		Model 4[d] (n = 16,738)	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Demographic variables[e]										
Age (per 10 years)	1.30	1.25, 1.35	1.41	1.36, 1.48	1.36	1.30, 1.43	1.30	1.24, 1.37	1.24	1.18, 1.31
Female gender	1.20	1.11, 1.31	1.09	1.00, 1.19	1.04	0.95, 1.14	1.06	0.96, 1.18	0.96	0.87, 1.07
Black race	3.31	3.05, 3.60	3.64	3.34, 3.97	3.27	2.97, 3.60	2.91	2.63, 3.22	2.78	2.50, 3.10
Living in the stroke belt[f] vs. other region	1.20	1.10, 1.30	1.37	1.26, 1.50	1.30	1.18, 1.43	1.25	1.13, 1.37	1.23	1.11, 1.36
Socioeconomic variables[e]										
Education less than high school	2.03	1.82, 2.26			1.21	1.06, 1.38	1.12	0.98, 1.29	1.12	0.97, 1.29
Annual income										
<$25,000	2.57	2.28, 2.91			1.42	1.24, 1.63	1.24	1.07, 1.42	1.18	1.02, 1.37
$25,000–$75,000	1.80	1.62, 2.01			1.29	1.15, 1.44	1.22	1.09, 1.38	1.18	1.04, 1.33
>$75,000[g]	1.00				1.00		1.00		1.00	
Medical conditions[e]										
Vascular disease	1.80	1.64, 1.96					1.45	1.30, 1.62	1.29	1.15, 1.45
Diabetes	3.08	2.82, 3.35					2.18	1.96, 2.41	2.09	1.87, 2.33
Hypertension	2.15	1.97, 2.35					1.32	1.19, 1.47	1.15	1.03, 1.28
Ever smoker	0.83	0.77, 0.90					0.78	0.71, 0.86	0.76	0.69, 0.84
Body mass index (per 5 kg/m^2)	1.16	1.13, 1.20					1.00	0.99, 1.01	0.99	0.98, 1.00
Anemia-associated conditions[e]										
Chronic kidney disease	4.01	3.62, 4.43							3.55	3.13, 4.04
Inflammation	2.38	2.12, 2.66							1.75	1.52, 2.02
Microcytosis	7.28	6.34, 8.38							5.76	4.87, 6.80

Abbreviations: CI, confidence interval; OR, odds ratio; REGARDS, REasons for Geographic And Racial Differences in Stroke.

[a] Model 1: age (per 10 years), female gender (yes/no), race (black vs. white), region (stroke belt vs. other).

[b] Model 2: model 1 + education less than high school (yes/no), annual income (<$25,000, $25,000–$75,000, >$75,000).

[c] Model 3: model 2 + vascular disease (yes/no), diabetes (yes/no), hypertension (yes/no), ever smoker (yes/no), body mass index (per 5 kg/m^2).

[d] Model 4: model 3 + chronic kidney disease (glomerular filtration rate <60 mL/minute per 1.73 m^2), inflammation (C-reactive protein ≥10 mg/dL or leukocyte count $\geq 15 \times 10^9$/L), and microcytosis (mean corpuscular volume <80 fL).

[e] Definitions are provided in the Materials and Methods section of the text.

[f] North Carolina, South Carolina, Georgia, Tennessee, Alabama, Mississippi, Arkansas, Louisiana.

[g] Reference category.

hypertension were associated with anemia in all models, with some reduction in the odds ratios in adjusted models. Of the medical conditions, diabetes was most strongly associated with anemia, an association not accounted for after adjustment for chronic kidney disease. Current or former smoking was inversely associated with anemia in all models (Table 4).

In unadjusted models, chronic kidney disease, inflammation, and microcytosis were associated with anemia, with microcytosis associated with a 7-fold increased odds of anemia (Table 4). In the fully adjusted model, the odds of anemia were 3.55-fold for participants with chronic kidney disease, 1.75-fold for participants with inflammation, and 5.76-fold for participants with microcytosis.

Table 5 shows that associations of age, vascular disease, and diabetes with anemia were significantly weaker for blacks than whites (P for interaction = 0.046, 0.018, and <0.001, respectively). Microcytosis was much more strongly associated with anemia in whites than blacks, although only 109 anemic whites had microcytosis. Other associations of risk factors with anemia were similar between the racial groups.

DISCUSSION

Anemia was nearly 3 times more common in American blacks than whites in this national cohort, and only part of this racial difference was explained by differences in risk factors for anemia. Compared with whites with anemia, blacks with anemia had a lower prevalence of chronic kidney disease and a higher prevalence of inflammation and microcytosis. Older age, lower income, vascular disease,

Table 5. Race-Stratified Multivariable Logistic Regression Model of Anemia Correlates in the REGARDS Renal Ancillary Study,[a] United States, 2003–2007

	Black (n = 6,733)		White (n = 10,005)	
	OR	95% CI	OR	95% CI
Demographic variables				
Age (per 10 years)[b]	1.19	1.11, 1.27	1.32	1.21, 1.44
Female gender	1.00	0.87, 1.15	0.92	0.78, 1.09
Living in the stroke belt[c] vs. other region	1.23	1.08, 1.40	1.19	1.01, 1.40
Socioeconomic variables				
Education less than high school	1.20	1.02, 1.42	0.98	0.73, 1.31
Annual income				
<$25,000	1.25	1.03, 1.51	1.01	0.78, 1.31
$25,000–$75,000	1.20	1.02, 1.42	1.14	0.95, 1.37
>$75,000[d]	1.00		1.00	
Medical conditions				
Vascular disease[b]	1.19	1.02, 1.39	1.38	1.16, 1.65
Diabetes[b]	1.78	1.57, 2.03	2.86	2.37, 3.44
Hypertension	1.16	1.00, 1.34	1.13	0.95, 1.34
Ever smoker	0.71	0.63, 0.81	0.86	0.73, 1.01
Body mass index (per 5 kg/m^2)	1.00	0.99, 1.01	0.97	0.96, 0.99
Anemia category				
Chronic renal insufficiency	3.24	2.69, 3.89	4.03	3.36, 4.83
Inflammation	1.55	1.31, 1.84	2.13	1.66, 2.73
Microcytosis	3.97	3.31, 4.76	25.62	17.54, 37.40

Abbreviations: CI, confidence interval; OR, odds ratio; REGARDS, REasons for Geographic And Racial Differences in Stroke.

[a] All factors listed in this table were included in the model. Variables are defined in the Materials and Methods section of the text.

[b] Interaction terms between race and age, vascular disease, and diabetes were 0.046, 0.018, and 0.0004, respectively. Other interaction-term P values were >0.05.

[c] North Carolina, South Carolina, Georgia, Tennessee, Alabama, Mississippi, Arkansas, Louisiana.

[d] Reference category.

diabetes, hypertension, never smoking, chronic kidney disease, inflammation, and microcytosis were all associated with a higher prevalence of anemia. Older age, vascular disease, and diabetes had weaker associations with anemia in blacks than whites. Socioeconomic and other risk factors were similarly associated with anemia in blacks and whites.

These data agree with and extend prior research into black-white differences in anemia prevalence in the United States. Observations of lower hemoglobin levels among blacks have persisted in the United States for many years and are consistent with the data presented here (2, 5, 7). Very few studies have addressed the effect of both socioeconomic and medical conditions on the association of race with anemia. Among 1,744 individuals in the Duke Established Populations for Epidemiologic Studies of the Elderly cohort (including 936 blacks), blacks had a 3-fold higher prevalence of anemia compared with whites after adjustment for age, educational level, body mass index, eGFR, hospitalizations, institutionalization, and a composite health condition score (1). In the Duke cohort, individual associations of risk factors with anemia were not reported, and racial differences in the associations of risk factors with anemia were not studied. Previous studies have reported an association between black race and anemia after adjusting for economic factors (10) or comorbid conditions (13), but not both simultaneously. In REGARDS, only a small portion of the increased prevalence of anemia seen in blacks was mediated by the variables studied, suggesting that other unknown factors explain most of this race difference.

Some insight into the independent correlates of anemia can be gained from this analysis. Age, race, vascular disease, diabetes, chronic kidney disease, and inflammation remained associated with anemia, with little attenuation in the fully adjusted models, suggesting that these associations are independent of other subject characteristics. Associations of gender, hypertension, and higher body mass index with anemia were substantially attenuated in the adjusted models, suggesting that the univariate associations of these factors with anemia were largely explained by other variables in the model. Diabetes was the strongest correlate of anemia in blacks and whites in this study, even after adjusting for renal function. The association of diabetes with

anemia independent of renal function has been reported in patients with decreased glomerular filtration rate (25). This finding may represent difficulties with eGFR calculations in assessing renal damage from diabetes, use of medications by diabetics that influence hemoglobin, or novel mechanisms related to diabetes. The 20% increased prevalence of anemia in the southeastern stroke-belt states was partly explained by socioeconomic variables and medical conditions but still retained significance in the final model. This novel finding highlights the need for further research on regional health differences in the United States.

Some correlates of anemia differed by race; prevalent vascular disease, diabetes, and increasing age were more strongly associated with anemia in whites than blacks, whereas socioeconomic factors were similarly associated with anemia in blacks and whites. These results were unexpected. In a recent analysis of Medicare health plans, blacks with coronary artery disease, diabetes, and hypertension had significantly lower rates of achieving quality-of-care goals than did whites (15). It follows that if diabetes, hypertension, and vascular disease cause anemia and were less well managed among blacks, they might also have stronger associations with anemia in blacks. We used the presence or absence of medical conditions in modeling, which may not capture racial differences in level of control of these conditions. In addition, there may be a common risk factor for anemia in blacks not assessed here, diluting the associations of medical conditions with anemia.

Whether there should be race-specific hemoglobin definitions of anemia, in addition to gender-specific definitions, is controversial. The World Health Organization criteria were never meant to serve as an exacting reference standard. Their report states that ''[t]hese figures were chosen arbitrarily and it is still not possible to define normal precisely'' (23, p. 9). In an effort to define gender- and race-specific hemoglobin ranges, Beutler and Waalen (26) calculated normal ranges for hemoglobin in blacks and whites in 2 studies that included fewer blacks than in REGARDS, the Scripps-Kaiser database ($n = 1{,}029$ blacks), and the Third National Health and Nutrition Examination Survey ($n = 2{,}834$ blacks). In this analysis, the 2.5th- and 5th-percentile cutoffs for black men and women were approximately 1g/dL lower than for white men and women, similar to our findings. Arguing against using race- and gender-specific criteria are outcomes data from the Cardiovascular Health Study and the Duke Established Populations for Epidemiologic Studies of the Elderly cohorts suggesting that black mortality is similar to that of whites in relation to anemia defined by the World Health Organization criteria (1, 2), although the opposite was found in a recent analysis of the Health, Aging, and Body Composition Study, where blacks were found to tolerate anemia better than whites in terms of mortality (9). More outcomes studies that include large black populations with data on the causes of anemia are needed to answer this question.

In this study, anemia-associated conditions differed by race. Among those with anemia, blacks had a lower prevalence of chronic kidney disease than whites, despite having a higher prevalence of conditions such as diabetes and hypertension that put them at risk of chronic kidney disease. This finding could be due to difficulties in calculating glomerular filtration rate using creatinine-based formulas, and the association may weaken if other markers of kidney disease such as proteinuria or cystatin C are taken into account (24). Of those with anemia, blacks were more likely to have inflammation and microcytosis. In the Third National Health and Nutrition Examination Survey, one-third of anemia was attributed to nutritional deficiencies and one-third to severe kidney disease (glomerular filtration rate <30 mL/minute per 1.73 m^2) and chronic inflammation; the rest was unclassified (7). The authors reported that anemia due to chronic inflammation and unclassified anemia were more common in blacks, but the total number of individuals in this analysis was too small for a detailed analysis of black-white differences in anemia (7). There are few reports on causes of anemia and outcomes; however, in a recent report, anemia associated with a low glomerular filtration rate was better tolerated than anemia associated with a normal glomerular filtration rate (4). The individuals studied were all from Calgary, Canada; were elderly; and were primarily white. Whether this finding is generalizable to diverse geographic and racial populations requires further study, particularly in blacks, whom we found to have a lower prevalence of chronic kidney disease than whites with anemia.

Some limitations of this study relate to its cross-sectional design. Causality could not be established, anemia was assessed at only one time point, and there was no follow-up to assess clinical impact. Some risk factors for anemia were not assessed (such as bleeding history, prior history of anemia, iron indices, or vitamin levels), and the specific cause of anemia was unknown. We did not have data on inherited hemoglobin variants such as α-thalassemia or sickle cell trait. α-Thalassemia trait does cause lower hemoglobin concentrations (but not anemia) and microcytosis. In an analysis by Beutler and West (8), α-thalassemia trait was thought to explain about one-third of the difference in hemoglobin concentrations between blacks and whites. In our sensitivity analyses, black race was still strongly associated with anemia in the REGARDS study when we removed data for those with microcytosis from the analysis or when mean corpuscular volume was included in the models as a continuous variable, so we might anticipate a small impact of α-thalassemia trait on the observed associations. We do not think that sickle cell disease or trait would impact our findings because sickle cell trait is not associated with lower hemoglobin or mean corpuscular volume. Sickle cell anemia would not be common in this middle-to-older-aged cohort because of the decreased lifespan and comorbidities of sickle cell anemia (8).

In summary, we found a substantial difference in anemia prevalence and hemoglobin levels in blacks and whites. Correlates of anemia and anemia-associated conditions differed by race. Although we did not find one specific cause for the difference in anemia prevalence in blacks and whites, socioeconomic factors and medical conditions such as vascular disease, diabetes, and hypertension explained part of the association, and they are modifiable. Ensuring quality medical care regardless of race, income, or education might reduce the racial disparity in anemia prevalence. Surprisingly, diabetes, vascular disease, and age were less

associated with anemia in blacks than in whites. These data highlight the need for further research into the differing causes of anemia in blacks and whites and whether improved management of medical conditions in those with anemia could reduce the difference in anemia prevalence among blacks and whites.

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